

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) An isolated and purified nucleic acid sequence comprising a polynucleotide sequence encoding a polypeptide of an antibody-~~(or fragment thereof)~~, wherein said antibody-~~(or fragment thereof)~~-has binding affinity to a p53 protein or a portion thereof in vertebrates, and wherein said nucleic acid sequence is obtained from a vertebrate host expressing an immune response against a naturally-occurring disease.
2. (Currently Amended) A-The nucleic acid sequence according to claim 1, wherein said immune response is ~~characterised~~ characterized by expression of at least one p53 antibody.
3. (Currently Amended) A-The nucleic acid sequence according to claim 1 ~~or claim 2~~ comprising a polynucleotide sequence encoding an F_{ab} antibody fragment-~~(or fragment thereof)~~ having binding affinity to a p53 protein or a portion thereof in vertebrates.
4. (Currently Amended) An isolated and purified nucleic acid sequence encoding a polypeptide of an antibody-~~(or fragment thereof)~~-comprising a polynucleotide sequence selected from the group consisting of SEQ ID Nos 1-30, wherein said antibody-~~(or fragment thereof)~~-has binding affinity to a p53 protein or a portion thereof.
5. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~ claim 1 to 4, wherein the nucleic acid sequence is DNA.
6. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~ claim 1 to 4, wherein the nucleic acid sequence is RNA.
7. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~ claim 1 to 6, wherein the nucleic acid sequence comprises a polynucleotide sequence-~~(s)~~ or sequences, or an analogue thereof, encoding an antibody fragment or other immunologically active fragment thereof, :

wherein the antibody-(~~or fragment thereof,~~) has binding affinity to a p53 protein or a portion thereof in vertebrates.

8. (Currently Amended) AThe nucleic acid sequence according to claim 7, wherein the antibody fragment or other immunologically active fragment comprises at least one complementarity determining region.

9. (Currently Amended) AThe nucleic acid sequence according to claim 7-~~or claim 8,~~ wherein the antibody fragment comprises at least one functional antigen-binding domain.

10. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 7-~~to 9,~~ wherein the antibody fragment is selected from the group consisting of: Fv, F_{ab}, F(ab)₂, scFv (single chain Fv), dAb (single domain antibody), bi-specific antibodies, diabodies and triabodies.

11. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 1-~~to 10,~~ wherein the antibody-(~~or fragment thereof,~~) has binding affinity for residues of one or more of the N-terminus, the C-terminus or the central domain of a p53 protein or a portion thereof.

12. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 1-~~to 11,~~ wherein the antibody-(~~or fragment thereof,~~) has binding affinity for residues of the N-terminus of a p53 protein or a portion thereof.

13. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 1-~~to 12,~~ wherein the antibody-(~~or fragment thereof,~~) has binding affinity for residues about 10 to about 55 of the N-terminus of a p53 protein or portion thereof.

14. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 1-~~to 12,~~ wherein the antibody-(~~or fragment thereof,~~) has binding affinity for residues about 10 to about 25 of the N-terminus of a p53 protein or portion thereof.

15. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 1 to 12, wherein the antibody-(or fragment thereof)- has binding affinity for residues about 40 to about 50 of the N-terminus of a p53 protein or portion thereof.

16. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 1 to 12, wherein the antibody-(or fragment thereof)- has binding affinity for residues about 27 to about 44 of the N-terminus of a p53 protein or portion thereof.

17. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 1 to 12, wherein the antibody-(or fragment thereof)- has binding affinity for residues about 40 to about 44 of the N-terminus of a p53 protein or portion thereof.

18. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 1 to 11, wherein the antibody-(or fragment thereof)- has binding affinity for residues of the central domain of a p53 protein or a portion thereof.

19. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 1 to 18, wherein said sequence comprises a polynucleotide sequence encoding a polypeptide of an antibody (or fragment thereof)- having binding affinity to a p53 protein or a portion thereof in vertebrates, wherein said polynucleotide sequence encodes an immunoglobulin light chain variable region polypeptide or an immunoglobulin heavy chain variable region polypeptide.

20. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 1 to 19, wherein said sequence comprises a polynucleotide sequence encoding a polypeptide of an antibody (or fragment thereof)- having binding affinity to a p53 protein or a portion thereof in vertebrates, wherein said nucleic acid sequence comprises a first polynucleotide sequence encoding an immunoglobulin light chain variable region polypeptide, and a second polynucleotide sequence encoding an immunoglobulin heavy chain variable region polypeptide.

21. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 1 to 20, wherein the vertebrate is selected from the group consisting of human, non-human primate, murine, bovine, ovine, equine, caprine, leporine, avian, feline and canine.

22. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 1 to 21, wherein the vertebrate is human.

23. (Currently Amended) An isolated and purified nucleic acid sequence comprising an analogue of the nucleic acid sequence according to ~~any one of claims~~claim 1 to 22, wherein said analogue encodes a polypeptide having a biological activity which is functionally the same as the polypeptide (s) encoded by said polynucleotide sequence.

24. (Currently Amended) AThe nucleic acid sequence according to ~~any one of claims~~claim 1 to 23, wherein the disease is selected from the group consisting of cancer, rheumatoid arthritis and coronary heart disease.

25. (Currently Amended) AThe nucleic acid sequence according to claim 24, wherein the disease is cancer.

26. (Currently Amended) AThe nucleic acid sequence according to claim 25, wherein the cancer is selected from the group consisting of carcinogenic ~~tumour~~tumors; ~~tumours~~ tumors of epithelial origin, such as colo-rectal cancer, breast cancer, lung cancer, head and neck ~~tumour~~tumors, hepatic cancer, pancreatic cancer, ovarian cancer, gastric cancer, brain cancer, bladder cancer, prostate cancer and urinary/genital tract cancer, oesophageal cancer; mesenchymal ~~tumour~~tumors, such as sarcoma; and haemopoietic ~~tumour~~tumors, such as B cell lymphoma.

27. (Currently Amended) A polypeptide of an antibody ~~(_ or fragment thereof)~~, having binding affinity to a p53 protein or a portion thereof in vertebrates, wherein said polypeptide is obtained from a vertebrate host expressing an immune response against a naturally-occurring disease.

28. (Currently Amended) ~~A~~The polypeptide according to claim 27, wherein said immune response is ~~characterised~~characterized by expression of at least one p53 antibody.

29. (Currently Amended) An isolated and purified polypeptide, wherein said polypeptide is encoded by the nucleic acid sequence according to ~~any one of claims~~claims 1 to 26.

30. (Currently Amended) An isolated and purified polypeptide of an antibody-~~(, or fragment thereof),~~ comprising an amino acid sequence selected from the group consisting of SEQID Nos 31-60, wherein said antibody-~~(, or fragment thereof),~~ has binding affinity to a p53 protein or a portion thereof.

31. (Currently Amended) A polypeptide according to ~~any one of claims~~claim 27 to 30, wherein said polypeptide is selected from the group consisting of: Fv, F_{ab}, F(ab)₂, scFv (single chain Fv), dAb (single domain antibody), bi-specific antibodies, diabodies and triabodies.

32. (Currently Amended) ~~A~~The polypeptide according to ~~any one of claims~~claim 27 to 31, wherein said polypeptide has binding affinity to a p53 protein or a portion thereof.

33. (Currently Amended) ~~A~~The polypeptide according to ~~any one of claims~~claim 27 to 32, wherein said polypeptide has binding affinity for residues of one or more of the N-terminus, the C-terminus or the central domain of a p53 protein or a portion thereof.

34. (Currently Amended) ~~A~~The polypeptide according to ~~any one of claims~~claim 27 to 33, wherein said polypeptide has binding affinity for residues of the N-terminus of a p53 protein or a portion thereof.

35. (Currently Amended) ~~A~~The polypeptide according to ~~any one of claims~~claim 27 to 34, wherein said polypeptide has binding affinity for residues about 10 to about 55 of the N-terminus of a p53 protein or portion thereof.

36. (Currently Amended) A~~The~~ polypeptide according to ~~any one of claims~~claim 27 to 34, wherein said polypeptide has binding affinity for residues about 10 to about 25 of the N-terminus of a p53 protein or portion thereof.

37. (Currently Amended) A~~The~~ polypeptide according to ~~any one of claims~~claim 27 to 34, wherein said polypeptide has binding affinity for residues about 40 to about 50 of the N-terminus of a p53 protein or portion thereof.

38. (Currently Amended) A~~The~~ polypeptide according to ~~any one of claims~~claim 27 to 34, wherein said polypeptide has binding affinity for residues about 27 to about 44 of the N-terminus of a p53 protein or portion thereof.

39. (Currently Amended) A~~The~~ polypeptide according to ~~any one of claims~~claim 27 to 34, wherein said polypeptide has binding affinity for residues about 40 to about 44 of the N-terminus of a p53 protein or portion thereof.

40. (Currently Amended) A~~The~~ polypeptide according to ~~any one of claims~~claim 27 to 33, wherein said polypeptide has binding affinity for residues of the central domain of a p53 protein or a portion thereof.

41. (Currently Amended) An isolated and purified polypeptide, wherein said polypeptide is a homologous polypeptide of the polypeptide according to ~~any one of claims~~claim 27 to 40.

42. (Currently Amended) A~~The~~ polypeptide according to claim 41, wherein said polypeptide is at least 45% homologous to ~~the~~a polypeptide according to any one of claims 27 to 40, of an antibody or fragment thereof, having binding affinity to a p53 protein or a portion thereof in vertebrates, wherein said polypeptide of an antibody is obtained from a vertebrate host expressing an immune response against a naturally-occurring disease.

43. (Currently Amended) AThe polypeptide according to claim 41, wherein said polypeptide is at least 75% homologous to the polypeptide of an antibody, or fragment thereof, having binding affinity to a p53 protein or a portion thereof in vertebrates, wherein said polypeptide of an antibody is obtained from a vertebrate host expressing an immune response against a naturally-occurring disease ~~according to any one of claims 27 to 40.~~

44. (Currently Amended) AThe polypeptide according to claim 41, wherein said polypeptide is at least 95-99% homologous to the polypeptide of an antibody, or fragment thereof, having binding affinity to a p53 protein or a portion thereof in vertebrates, wherein said polypeptide of an antibody is obtained from a vertebrate host expressing an immune response against a naturally-occurring disease ~~according to any one of claims 27 to 40.~~

45. (Currently Amended) AThe polypeptide according to ~~any one of claims~~claim 27 ~~to 44~~, wherein the disease is selected from the group consisting of cancer, rheumatoid arthritis and coronary heart disease.

46. (Currently Amended) AThe polypeptide according to claim 45, wherein the disease is cancer.

47. (Currently Amended) AThe polypeptide according to claim 46, wherein the cancer is selected from the group consisting of carcinogenic ~~tumours~~tumors; ~~tumours~~tumors of epithelial origin, such as colo-rectal cancer, breast cancer, lung cancer, head and neck-~~tumours~~tumors, hepatic cancer, pancreatic cancer, ovarian cancer, gastric cancer, brain cancer, bladder cancer, prostate cancer and urinary/genital tract cancer, oesophageal cancer; mesenchymal-~~tumours~~tumors, such as sarcoma; and haemopoietic-~~tumours~~tumors, such as B cell lymphoma.

48. (Original) A peptide fragment of the polypeptide of any one of SEQ ID Nos 31-60, wherein said peptide fragment induces an immune response when administered to a vertebrate.

49. (Currently Amended) AThe peptide fragment according to claim 48, wherein said peptide fragment comprises between about 5 and about 50 contiguous amino acids of any one of SEQ ID Nos 31-60.

50. (Currently Amended) AThe peptide fragment according to ~~any one of claims~~claim 48 to 49, wherein said peptide fragment comprises between about 5 and about 30 contiguous amino acids of any one of SEQ ID Nos 31-60.

51. (Currently Amended) AThe peptide fragment according to ~~any one of claims~~claim 48 to 50, wherein said peptide fragment comprises between about 8 and about 20 contiguous amino acids of any one of SEQ ID Nos 31-60.

52. (Currently Amended) AThe peptide fragment according to claim 48, wherein said peptide fragment is derived from the complementarity determining region.

53. (Currently Amended) AThe peptide fragment according to ~~any one of claims~~claim 48 to 52, wherein said immune response is an idiotypic response.

54. (Currently Amended) AThe peptide fragment according to ~~any one of claims~~claim 48 to 53, wherein the vertebrate is human.

55. (Original) An antibody or fragment thereof, wherein said antibody or fragment thereof has binding affinity to a p53 protein or a portion thereof in vertebrates, and wherein said antibody is obtained from a vertebrate host expressing an immune response against a naturally-occurring disease.

56. (Currently Amended) AThe antibody or fragment thereof according to claim 55, wherein said immune response is ~~characterised~~characterized by expression of a p53 antibody.

57. (Currently Amended) ~~An~~The antibody, or fragment thereof, having binding affinity to a p53 protein or a portion thereof in vertebrates, wherein said antibody or fragment thereof is comprised of the polypeptide according to ~~any one of claims~~claim 27 to 47.

58. (Currently Amended) ~~An~~The antibody, or fragment thereof, having binding affinity to a p53 protein or a portion thereof in vertebrates, wherein said antibody or fragment thereof is encoded by the nucleic acid sequence according to ~~any one of claims~~claim 1 to 26.

59. (Currently Amended) ~~An~~The antibody fragment according to ~~any one of claims~~claim 55 to 58, wherein said fragment is an immunologically active fragment.

60. (Currently Amended) ~~An~~The antibody fragment according to ~~any one of claims~~claim 55 to 59, wherein said fragment comprises at least one complementarity determining region.

61. (Currently Amended) ~~An~~The antibody fragment according to ~~any one of claims~~claim 55 to 60, wherein said fragment is selected from the group consisting of: Fv, F_{ab}, F(ab)₂, scFv (single chain Fv), dAb (single domain antibody), bi-specific antibodies, diabodies and triabodies.

62. (Currently Amended) ~~An~~The antibody, or fragment thereof, according to ~~any one of claims~~claim 55 to 61, which is a polyclonal antibody.

63. (Currently Amended) ~~An~~The antibody, or fragment thereof, according to ~~any one of claims~~claim 55 to 61, which is a monoclonal antibody.

64. (Currently Amended) ~~An~~The antibody or fragment thereof according to ~~any one of claims~~claim 57 to 63, wherein said antibody or fragment thereof has binding affinity for residues of one or more of the N-terminus, the C-terminus or the central domain of a p53 protein or a portion thereof.

65. (Currently Amended) ~~Any~~The antibody or fragment thereof according to ~~any one of claims~~claim 57 to 64, wherein said antibody or fragment thereof has binding affinity for residues of the Nterminus of a p53 protein or a portion thereof.

66. (Currently Amended) ~~Any~~The antibody or fragment thereof according to ~~any one of claims~~claim 57 to 65, wherein said antibody or fragment thereof has binding affinity for residues about 10 to about 55 of the N-terminus of a p53 protein or portion thereof.

67. (Currently Amended) ~~Any~~The antibody or fragment thereof according to ~~any one of claims~~claim 57 to 65, wherein said antibody or fragment thereof has binding affinity for residues about 10 to about 25 of the N-terminus of a p53 protein or portion thereof.

68. (Currently Amended) ~~Any~~The antibody or fragment thereof according to ~~any one of claims~~claim 57 to 65, wherein said antibody or fragment thereof has binding affinity for residues about 40 to about 50 of the N-terminus of a p53 protein or portion thereof.

69. (Currently Amended) ~~Any~~The antibody or fragment thereof according to ~~any one of claims~~claim 57 to 65, wherein said antibody or fragment thereof has binding affinity for residues about 27 to about 44 of the N-terminus of a p53 protein or portion thereof.

70. (Currently Amended) ~~Any~~The antibody or fragment thereof according to ~~any one of claims~~claim 57 to 65, wherein said antibody or fragment thereof has binding affinity for residues about 40 to about 44 of the N-terminus of a p53 protein or portion thereof.

71. (Currently Amended) ~~Any~~The antibody or fragment thereof according to ~~any one of claims~~claim 57 to 64, wherein said antibody or fragment thereof has binding affinity for residues of the central domain of a p53 protein or a portion thereof.

72. (Currently Amended) ~~A~~The antibody or fragment thereof according to ~~any one of claims~~claim 55 to 71, wherein the disease is selected from the group consisting of cancer, rheumatoid arthritis and coronary heart disease.

73. (Currently Amended) ~~A~~The antibody or fragment thereof according to claim 72, wherein the disease is cancer.

74. (Currently Amended) ~~A~~The antibody or fragment thereof according to claim 73, wherein the cancer is selected from the group consisting of carcinogenic ~~tumour~~tumors; ~~tumours~~tumors of epithelial origin, such as colo-rectal cancer, breast cancer, lung cancer, head and neck ~~tumour~~tumors, hepatic cancer, pancreatic cancer, ovarian cancer, gastric cancer, brain cancer, bladder cancer, prostate cancer and urinary/genital tract cancer, oesophageal cancer; mesenchymal ~~tumour~~tumors, such as sarcoma; and haemopoietic ~~tumour~~tumors, such as B cell lymphoma.

75. (Currently Amended) A vector comprising the nucleic acid sequence according to ~~any one of~~claim 1 to 26.

76. (Currently Amended) ~~A~~The vector according to claim 75, wherein said vector is selected from the group consisting of viral, plasmid, bacteriophage, phagemid, cosmid, bacterial artificial chromosome, and yeast artificial chromosome.

77. (Currently Amended) ~~A~~The vector according to claim 76, wherein said bacteriophage is selected from the group consisting of λ gt10 and λ gt11 and phage display vectors.

78. (Currently Amended) ~~A~~The vector according to claim 77, wherein said phage display vector is selected from vectors derived from pCOMB vectors.

79. (Currently Amended) ~~A~~The vector according to claim 76 ~~or 77~~, wherein said phage display vector is of the MCO group.

80. (Currently Amended) ~~A~~The vector according to any one of claims ~~77 to 79~~, wherein said phage display vector is selected from the group consisting of MCO1, MCO3 and MCO6 vectors.

81. (Currently Amended) ~~A~~The vector according to ~~any one of claims~~claim ~~77 to 80~~, wherein said phage display vector is MCO3.

82. (Currently Amended) ~~A~~The vector according to claim 75, wherein said vector is a mammalian expression vector.

83. (Currently Amended) ~~A~~The vector according to claim 82, wherein said mammalian expression vector is pG1D102-MCO or pKN100-MCO.

84. (Currently Amended) A host cell transformed with the vector according to ~~any one of claims~~claim ~~75 to 83~~.

85. (Currently Amended) ~~A~~The host cell according to claim 84, wherein said host cell is selected from the group consisting of *E. coli*, *Bacillus*, *Streptomyces*, *Pseudomonas*, *Salmonella*, and *Serratia*.

86. (Currently Amended) ~~A~~The host cell according to claim 84, wherein said host cell is selected from the group consisting of yeast, fungi, plant, insect cells and mammalian cells.

87. (Currently Amended) ~~A~~The host cell according to claim 86, wherein said mammalian cells are selected from the group consisting of CHO cell lines, COS cell lines, HeLa cells, L cells, murine 3T3 cells, c6 glioma cells and myeloma cell lines.

88. (Currently Amended) ~~A~~The host cell according to claim ~~86 or claim 87~~, wherein said mammalian cells are CHO DG44 cells.

89. (Currently Amended) A non-human vertebrate comprising a host cell according to ~~any one of claims~~claim 84 to 88.

90. (Currently Amended) A pharmaceutical composition comprising the polypeptide according to ~~any one of claims~~claim 27 to 47, ~~or a peptide fragment according to any one of claims 48 to 54, or an antibody or fragment thereof according to any one of claims 55 to 74,~~ together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

91. (Currently Amended) AThe pharmaceutical composition according to claim 90, wherein said polypeptide is in a form selected from the group consisting of polypeptide/chelate, polypeptide/drug, polypeptide/prodrug, polypeptide/toxin, polypeptide/imaging marker, antibody/chelate, antibody/drug, antibody/prodrug, antibody/toxin and antibody/imaging marker.

92. (Currently Amended) AThe pharmaceutical composition according to claim 91, wherein said chelate is selected from the group consisting of: ^{90}Y , ^{131}I and ^{188}Re .

93. (Currently Amended) AThe pharmaceutical composition according to claim 91, wherein said drug is a cytotoxic drug.

94. (Currently Amended) AThe pharmaceutical composition according to claim 93, wherein said cytotoxic drug is selected from the group consisting of adriamycin, melphalan, cisplatin, taxol, fluorouracil, cyclophosphamide.

95. (Currently Amended) AThe pharmaceutical composition according to claim 91, wherein said prodrug is an antibody directed prodrug therapy or ADEPT.

96. (Currently Amended) AThe pharmaceutical composition according to claim 91, wherein said toxin is selected from the group consisting of ricin, abrin, *Diphtheria* toxin and *Pseudomonas* endotoxin (PE 40).

97. (Currently Amended) ~~A~~The pharmaceutical composition according to claim 91, wherein said imaging marker is selected from the group consisting of ^{125}I , ^{131}I , ^{123}I , ^{111}In , ^{105}Rh , ^{153}Sm , ^{67}Cu , ^{166}Ho , ^{177}Lu , ^{186}Re , ^{188}Re , and $^{99\text{m}}\text{Tc}$.

98. (Currently Amended) ~~A~~The pharmaceutical composition according to claim 91, wherein said imaging marker is gadolinium.

99. (Currently Amended) A vaccine comprising a nucleic acid sequence according to ~~any one of claims~~claim 1 to 26, or a fragment thereof, ~~or a polypeptide according to any one of claims 27 to 47, or a peptide fragment according to any one of claims 48 to 54, or an antibody or fragment thereof according to any one of claims 55 to 74,~~ together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

100. (Currently Amended) ~~A~~The vaccine according to claim 99, wherein said vaccine is an idiotypic vaccine.

101. (Currently Amended) ~~A~~The vaccine according to claim 99 ~~or claim 100~~, wherein said vaccine is formulated for administration via an oral, inhalation, topical or parenteral route.

102. (Currently Amended) A method for inducing an immune response against disease in a vertebrate, comprising administering to said vertebrate an immunologically effective amount of the polypeptide ~~(or peptide fragment thereof),~~ according to ~~any one of claims~~claim 27 to 47, ~~or a peptide fragment according to any one of claims 48 to 54, or an antibody (or fragment thereof) according to any one of claims 55 to 74, or a pharmaceutical composition according to any one of claims 90 to 98, or a vaccine according to any one of claims 99 to 101.~~

103. (Currently Amended) The method according to claim 102, wherein the polypeptide, peptide fragment, or antibody ~~(or fragment thereof),~~ is administered together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

104. (Currently Amended) A method for the treatment and/or prophylaxis of disease in a vertebrate in need of said treatment and/or prophylaxis, wherein said method comprises administering to said vertebrate a therapeutically effective amount of the polypeptide ~~(, or peptide fragment thereof),~~ according to ~~any one of claims~~ claim 27 to 47, or the peptide fragment according to ~~any one of claims~~ 48 to 54, or an antibody (or fragment thereof) according to ~~any one of claims~~ 55 to 74, or a pharmaceutical composition according to ~~any one of claims~~ 90 to 98, or a vaccine according to ~~any one of claims~~ 99 to 101.

105. (Currently Amended) The method according to ~~any one of claims~~ claim 102 to 104, wherein the disease is selected from the group consisting of cancer, rheumatoid arthritis and coronary heart disease.

106. (Currently Amended) The method according to ~~any one of claims~~ claim 102 to 105, wherein the disease is cancer.

107. (Currently Amended) The method according to claim 106, wherein the cancer is selected from the group consisting of carcinogenic ~~tumour~~ tumors; ~~tumour~~ tumors of epithelial origin, such as colo-rectal cancer, breast cancer, lung cancer, head and neck ~~tumour~~ tumors, hepatic cancer, pancreatic cancer, ovarian cancer, gastric cancer, brain cancer, bladder cancer, prostate cancer and urinary/genital tract cancer, oesophageal cancer; mesenchymal ~~tumour~~ tumors, such as sarcoma; and haemopoietic ~~tumour~~ tumors, such as B cell lymphoma.

108. (Currently Amended) A diagnostic kit for the detection of polypeptides encoded by the p53 gene in vertebrates, said kit comprising the antibody ~~(, or fragment thereof),~~ according to ~~any one of claims~~ claim 55 to 74, together with a diagnostically acceptable carrier and/or diluent.

109. (Currently Amended) ~~A~~ The diagnostic kit according to claim 108, wherein said kit comprises:

(a) ___ a first container containing the antibody ~~(, or fragment thereof), wherein said antibody or fragment thereof has binding affinity to a p53 protein or a portion thereof in vertebrates, and wherein~~

said antibody is obtained from a vertebrate host expressing an immune response against a naturally-occurring disease according to any one of claims 55 to 74, -and;

(b) ____ a second container containing a conjugate comprising a binding partner of the antibody-(~~or fragment thereof~~), together with a detectable label.

110. (Currently Amended) A method for screening for a disease in a vertebrate comprising :

(a) ____ contacting a sample from a vertebrate with a nucleic acid probe comprising a nucleic acid sequence according to ~~any one of claims~~claim 1 ~~to 26~~, or an oligonucleotide fragment thereof, and

(b) ____ detecting ~~hybridisation~~-hybridization between the nucleic acid sample and the polynucleotide sequence.

111. (Currently Amended) AThe method according to claim 110, wherein the oligonucleotide fragment is between about 10 to about 100 nucleotides in length.

112. (Currently Amended) AThe method according to claim 110 ~~or claim 111~~, wherein the oligonucleotide fragment is between about 15 to about 30 nucleotides in length.

113. (Currently Amended) The method according to ~~any one of claims~~claim 110 ~~to 112~~, wherein ~~hybridisation~~-hybridization as compared to non-~~hybridisation~~hybridization is indicative of disease.

114. (Currently Amended) The method according to any one of claims 110 ~~to 113~~, wherein said disease is cancer.

115. (Currently Amended) The method according to ~~any one of claims~~claim 110 ~~to 114~~, wherein ~~hybridisation~~-hybridization is conducted under low, moderate, or high stringency.

116. (Currently Amended) The method according to ~~any one of claims~~claim 110 to 115, wherein ~~hybridisation~~hybridization is conducted under high stringency.

117. (Currently Amended) A method for screening for a disease in a vertebrate comprising:

(a) ___ contacting a sample from a vertebrate with the antibody ~~(or fragment thereof)~~, according to ~~any one of claims~~claim 55 to 74, and

(b) ___ detecting the presence of the antibody ~~(or fragment thereof)~~, bound to a p53 polypeptide.

118. (Currently Amended) ~~A~~The method according to claim 117, wherein said disease is cancer.

119. (Currently Amended) A method of gene therapy, wherein said method comprises:

(a) ___ inserting a nucleic acid sequence according to ~~any one of claims~~claim 1 to 26, or a vector according to ~~any one of claims~~ 75 to 83, into a host cell;

(b) ___ expressing the nucleic acid sequence in the transformed cell.

120. (Original) The method according to claim 119, wherein said vector is an expression vector.

121. (Currently Amended) A process for preparing an antibody ~~(or fragment thereof)~~, having binding affinity to a p53 protein or a portion thereof in vertebrates, wherein said process comprises:

(a) ___ isolating from a vertebrate a nucleic acid sequence according to ~~any one of~~
~~claims~~claim 1 to 26;

(b) ___ cloning said nucleic acid sequence into a vector;

(c) ____constructing an antibody fragment library; and

(d) ____screening said library for clones expressing the antibody of interest.

122. (Currently Amended) The process according to claim 121, wherein said antibody-~~_, or fragment thereof~~, has binding affinity to a p53 protein or a portion thereof in vertebrates.

123. (Original) The process according to claim 121, wherein said nucleic acid sequence is obtained from an organ suffering from or a collection point for expression of, the disease.

124. (Original) The process according to claim 123, wherein said organ is a lymph node.

125. (Currently Amended) The process according to ~~any one of claims~~claim 121 to 124, wherein the vector is a phage display vector.

126. (Original) The process according to claim 125, wherein the vector is selected from the group consisting of MC01, MC03 and MC06.

127. (Currently Amended) The process according to claim 125 ~~or claim~~126, wherein the vector is MC01.

128. (Currently Amended) A method of locating a nucleotide sequence encoding a polypeptide of an antibody-~~_, or fragment thereof~~, having binding affinity to a p53 protein or portion thereof in vertebrates, using the nucleic acid sequence according to ~~any one of claims~~claim 1 to 26, or an oligonucleotide fragment thereof.

129. (Currently Amended) The method according to claim 128, comprising:

(a) ____contacting a biological sample with a nucleic acid sequence according to comprising a polynucleotide sequence encoding a polypeptide of an antibody, or fragment thereof, wherein said antibody, or fragment thereof, has binding affinity to a p53

protein or a portion thereof in vertebrates, and wherein said nucleic acid sequence is obtained from a vertebrate host expressing an immune response against a naturally-occurring disease ~~any one of claims 1 to 26~~, or an oligonucleotide fragment thereof; and

(b) identifying nucleotide sequences in the biological sample which hybridise-hybridize to said nucleic acid sequence or oligonucleotide fragment.

130. (Currently Amended) ~~A~~The method according to claim 129, wherein the oligonucleotide fragment is between about 10 to about 100 nucleotides in length.

131. (Currently Amended) ~~A~~The method according to claim 129 ~~or claim 130~~, wherein the oligonucleotide fragment is between about 15 to about 30 nucleotides in length.

132. (New) A pharmaceutical composition comprising a peptide fragment according to claim 48 together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

133. (New) A pharmaceutical composition comprising an antibody or fragment thereof according to claim 55 together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

134. (New) A vaccine comprising a polypeptide according to claim 27 together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

135. (New) The vaccine according to claim 134, wherein said vaccine is an idiotypic vaccine.

136. (New) The vaccine according to claim 134, wherein said vaccine is formulated for administration via an oral, inhalation, topical or parenteral route.

137. (New) A vaccine comprising a peptide fragment according to claim 48 together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

138. (New) The vaccine according to claim 137, wherein said vaccine is an idiotypic vaccine.

139. (New) The vaccine according to claim 137, wherein said vaccine is formulated for administration via an oral, inhalation, topical or parenteral route.

140. (New) A vaccine comprising an antibody or fragment thereof according to claim 55, together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

141. (New) The vaccine according to claim 140, wherein said vaccine is an idiotypic vaccine.

142. (New) The vaccine according to claim 140, wherein said vaccine is formulated for administration via an oral, inhalation, topical or parenteral route.

143. (New) A method for inducing an immune response against disease in a vertebrate, comprising administering to said vertebrate an immunologically effective amount of the peptide fragment according to claim 48.

144. (New) The method according to claim 143, wherein the polypeptide, peptide fragment, or antibody, or fragment thereof, is administered together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

145. (New) A method for the treatment and/or prophylaxis of disease in a vertebrate in need of said treatment and/or prophylaxis, wherein said method comprises administering to said vertebrate a therapeutically effective amount of the peptide fragment according to claim 48.

146. (New) The method according to claim 143, wherein the disease is selected from the group consisting of cancer, rheumatoid arthritis and coronary heart disease.

147. (New) The method according to claim 143, wherein the disease is cancer.

148. (New) The method according to claim 147, wherein the cancer is selected from the group consisting of carcinogenic tumors; tumors of epithelial origin, such as colo-rectal cancer, breast cancer, lung cancer, head and neck tumors, hepatic cancer, pancreatic cancer, ovarian cancer, gastric cancer, brain cancer, bladder cancer, prostate cancer and urinary/genital tract cancer, oesophageal cancer; mesenchymal tumors, such as sarcoma; and haemopoietic tumors, such as B cell lymphoma.

149. (New) A method for inducing an immune response against disease in a vertebrate, comprising administering to said vertebrate an immunologically effective amount of the antibody, or fragment thereof, according to claim 55.

150. (New) The method according to claim 149, wherein the polypeptide, peptide fragment, or antibody, or fragment thereof, is administered together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

151. (New) A method for the treatment and/or prophylaxis of disease in a vertebrate in need of said treatment and/or prophylaxis, wherein said method comprises administering to said vertebrate a therapeutically effective amount of the antibody, or fragment thereof, according to claim 55.

152. (New) The method according to claim 149, wherein the disease is selected from the group consisting of cancer, rheumatoid arthritis and coronary heart disease.

153. (New) The method according to claim 149, wherein the disease is cancer.

154. (New) The method according to claim 153, wherein the cancer is selected from the group consisting of carcinogenic tumors; tumors of epithelial origin, such as colo-rectal cancer, breast cancer, lung cancer, head and neck tumors, hepatic cancer, pancreatic cancer, ovarian cancer, gastric cancer, brain cancer, bladder cancer, prostate cancer and urinary/genital tract cancer,

oesophageal cancer; mesenchymal tumors, such as sarcoma; and haemopoietic tumors, such as B cell lymphoma.

155. (New) A method for inducing an immune response against disease in a vertebrate, comprising administering to said vertebrate an immunologically effective amount of the pharmaceutical composition according to claim 90.

156. (New) The method according to claim 155, wherein the polypeptide, peptide fragment, or antibody, or fragment thereof, is administered together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

157. (New) A method for the treatment and/or prophylaxis of disease in a vertebrate in need of said treatment and/or prophylaxis, wherein said method comprises administering to said vertebrate a therapeutically effective amount of the pharmaceutical composition according to claim 90.

158. (New) The method according to claim 155, wherein the disease is selected from the group consisting of cancer, rheumatoid arthritis and coronary heart disease.

159. (New) The method according to claim 155, wherein the disease is cancer.

160. (New) The method according to claim 159, wherein the cancer is selected from the group consisting of carcinogenic tumors; tumors of epithelial origin, such as colo-rectal cancer, breast cancer, lung cancer, head and neck tumors, hepatic cancer, pancreatic cancer, ovarian cancer, gastric cancer, brain cancer, bladder cancer, prostate cancer and urinary/genital tract cancer, oesophageal cancer; mesenchymal tumors, such as sarcoma; and haemopoietic tumors, such as B cell lymphoma.

161. (New) A method for inducing an immune response against disease in a vertebrate, comprising administering to said vertebrate an immunologically effective amount of the vaccine according to claim 99.

162. (New) The method according to claim 161, wherein the polypeptide, peptide fragment, or antibody, or fragment thereof, is administered together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

163. (New) A method for the treatment and/or prophylaxis of disease in a vertebrate in need of said treatment and/or prophylaxis, wherein said method comprises administering to said vertebrate a therapeutically effective amount of the pharmaceutical composition according to claim 99.

164. (New) The method according to claim 161, wherein the disease is selected from the group consisting of cancer, rheumatoid arthritis and coronary heart disease.

165. (New) The method according to claim 161, wherein the disease is cancer.

166. (New) The method according to claim 165, wherein the cancer is selected from the group consisting of carcinogenic tumors; tumors of epithelial origin, such as colo-rectal cancer, breast cancer, lung cancer, head and neck tumors, hepatic cancer, pancreatic cancer, ovarian cancer, gastric cancer, brain cancer, bladder cancer, prostate cancer and urinary/genital tract cancer, oesophageal cancer; mesenchymal tumors, such as sarcoma; and haemopoietic tumors, such as B cell lymphoma.

167. (New) A method of gene therapy, wherein said method comprises:

- (a) inserting a vector according to claim 75 into a host cell;
- (b) expressing the nucleic acid sequence in the transformed cell.